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ON THE BIOLOGICAL EFFECTS OF HIGH ENERGY PROTONS

by

P. P. Saksonov
V. V. Antipov
V. S. Sharkov
..... and .....
V. S. Morozov

[USSR]

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by P. P. Saksonov
V. V. Antipov
V. S. Sharkov
..... & .....
V. S. Morozov

SUMMARY

This paper deals with the results of various experiments with mice and rats in regard to radiation-shielding properties of certain pharmaco-chemical agents during irradiation by protons with energies from 660 to 120 Mev, drawing comparison with the simultaneous action on animals by γ — rays.

The experiments have shown that optimum shieding effect was obtained with aminoethylisotiuron dihydrobromide (AET), 5— methoxytriptamine chlorhydrate and serotinin. When introducing these compounds, 50—70 percent of mice survived. by comparison with cystamine (~50%), triptamine and 5-oxytriptophan (~20%).

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The problem of biological effect of cosmic radiations on living organisms has not only a theoretical, but also a practical value. The cosmic radiation is one of the main barriers during prolonged space flights beyond the limits of the Earth's magnetic field [1— 3]. From the practical viewpoint particular interesting aspect of radiation danger is presented by the corpuscular radiations — high-energy protons and multiple-charge nuclei [4 — 7].

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*(O BIOLOGICHESKOM DEYSTVII PROTONOV VYSOKOY ENERGII)

It is usually admitted that in the presence of satisfactory information on the physical characteristics of cosmic radiation, the main obstacle for establishing scientifically founded and permissible radiation levels and the working out of effective protection measures in the absence of sufficient data on the relative biological effectiveness (RBE) of separate cosmic radiation components.

The RBE of various forms of radiations, including the corpuscular, depends on numerous factors. In this regard a great role is played by the ionization density and the linear losses of energy when radiations traverse the matter. It is well known that the specific ionization increase from 3 to 100 pairs of ions per 1μ of path is little reflected on the RBE, which remains approximately equal to the unity. The increase of ionization density from 100 to 1000 pairs of ions per 1μ gives a RBE increase proportionally to the logarithm of specific ionization [8]. It should be stressed, that in estimating the RBE alongside with various physical peculiarities of radiation effects, it is necessary to take also into the account the biological peculiarities, the organization level and the functional state of the cell, the organ, the system and of the organism. The character of the tests, with the aid of which the relative effectiveness of either form of radiations is determined, should also be taken into account.

It is well known that protons are the most widespread form of penetrating radiation in space. 85% of them are in the primary cosmic radiation (galactic rays), and they are generated in great amounts during solar chromospheric flares, entering in the content of the outer and the inner radiation belts.

Only first steps have so far been taken for the determination of the RBE of protons. According to data of E. B. Kurlyandskaya et al [9] and G. A. Avrunina [10], the biological effectiveness of protons was bound to be no higher than that of X-rays, and, according to some indicators, such as the mortality, the change in the morphological content of the peripheral blood, it may be even lower. Thus by $\alpha = D_{50}$, the RBE for mice is 0.55 and for rats — 0.65. A. V. Lebedinskiy et al [11] have established that the RBE factor of protons with energies of 510 Mev for rats is 0.8, and for dogs — 1.2.

Authors of [12] assume that RBE factor for protons with 730 Mev energy is, by comparison with γ— rays, about 2. This conclusion is made by them on the basis of experiments with monkeys, in which the RBE was estimated by the time of appearance, the weight of iridocyclitis flow, the erythema and various other damages to visual organs. According to [13] the RBE for protons of 157 Mev energy by $\alpha = D_{50}$ for mice constitutes 0.77 ± 0.1 by comparison with X-rays.

We present in the current work the results of experiments on studies of the RBE of protons with enery of 660 and 120 Mev, whose specific ionization is respectively 6 and 20 pairs of ions per 1μ (G. F. Murin, V. S. Morozov et al). The experiments were set up on various biological objects and different methods of investigation, The objects were subjected to a proton beam pulse from a synchrocyclotron of the Centralized Institute of Nuclear Investigations with a current density of $10^8 - 10^9$ particle per cm^2/sec. There were nearly 100 pulses of 200 — μsec duration, in one second. The power of the dose, determined by the imparted activity on the carbon plates, constitutes in our experiments 400 — 700 rad/min for E =660 Mev and 80 — 120 rad/min for E = 120 Mev. The relative biological effectiveness of protons by comparison with gamma rays was estimated by way of various tests, characterizing the vital activity and the heredity of the cell or organism.

The experiments conducted have shown, that the RBE for protons with energies of 660 and 120 Mev by DL_{50} for mice and rats constituted ~0.7. Clinical observations of animals have also shown a somewhat lesser effectiveness of protons by comparison with γ-rays (V. S. Shashkov, B. L. Razgovorov et al). Identical results were obtained during the comparative estimate of chromospheric disruptions in the marrow cells of mice (M. A. Arsen'yeva, L. A. Belyayeva et al), in germs of higher plants, such as wheat, peas, barley etc.. (V. V. Khvostova et al, L. K. Gordon), at determination of recessive, sex-linked and dominant flying mutations in Drosophila melanogaster (Ya. L. Glembotskiy, G. P. Parfenov et al).

It should be stressed, that during the estimate of high energy protons' RBE, obtained in various accelerators, it is necessary to take into account the pulse character of irradiation and the high-power doses.

These factors must necessarily influence the results of biological action of the radiation, and, consequently, they must be taken into account during an orienting determination of RBE of protons originating from primary cosmic radiation, the inner and outer radiation belts and the solar flares.

For a fuller appraisal of the RBE of protons, the results of experiments on the radio-shielding properties of certain pharmaco-chemical means, applied in conditions of irradiation by protons are of essential interest. It is entirely evident that such investigations are also indispensable when trying to resolve the question of principle related to the possibility of utilizing such compounds in conditions of action by corpuscular radiation. To these compounds we must, first of all, refer cysteamin, cystamin, serotinin, aminoethylisotiuron dihydrobromide (AET), 5-methoxytriptamine chlorhydrate and others.

The first experiments on the study of radio-shielding properties of various compounds or organism irradiation by protons were conducted by S. P. Yarmonenko et al [14]. In the experiments with mice it was shown that such compounds as cystamine, AET, serotinin and others are effective for X-rays and γ - rays, and they preserve their properties when animals are irradiated by protons with energies to 660 Mev.

In our experiments we also used radio-shielding properties of certain pharmaco-chemical compounds on mice and rats, when the latter were subject to action by protons with energies of 660 to 120 Mev. The effectiveness of these compounds was simultaneously checked with simultaneous irradiation of animals by γ - rays.

This paper has for object to bring up the results on tests of radio-shielding effect of cystamine bichloride (150 mg/kg), aminoethylisotiuron dihydrobromide (ART, 150 mg/kg), serotinin creatinsulphate (50 mg/kg), 5-methoxytriptamine chlorhydrate (75 mg/kg), triptamine chlorhydrate (100 mg/kg and 5-oxytriptophane (250 mg/kg). All the indicated compounds were introduced to animals internally about 15 to 30 minutes prior to irradiation. The doses of compounds are taken into account at the outset. Animals of sub-control and control groups were subject to action of γ -rays and protons in absolutely mortal doses.

As was shown by the experiments, the best protecting effect was revealed with AET, 5-methoxytriptamine chlorhydrate and serotonin. When introducing these compounds to test animal groups, 50 — 70% of mice have survived. The delays of protected animal perishing exceeded significantly the lifetime of the irradiated ones. When applying cystamin, near 50% survived, while with triptamine and 5-oxytriptophanem only near 20% of test animals survived.

Therefore, analyzing the literature data and the results of our own investigations, we may, first of all, reach the conclusion, that the RBE of protons with energies ranging from 660 to 120 Mev, determined in experiments with mice, rats, drosophiles, seeds and other biological objects, does not exceed 1. These facts corroborate quite satisfactorily the assumption, advanced by us, that the RBE should not exceed 1 for the indicated values of specific ionization, that is 6 — 20 ions pairs per 1 on the tissue. A RBE above the unity for protons of 510 Mev energy was revealed in experiments on dogs [11] and for protons of 730 Mev — in the experiments on monkeys [12]. Evidently, this discrepancy is to a known measure conditioned by animal form and tests, with the aid of which the RBE was estimated.

The results obtained provide also a basis to hope that the utilization of some compounds as means of shielding astronauts and the entire biocomplex from the damaging effect of high-energy protons, may offer good perspectives.

A great theoretical and practical interest for space biology and medicine must be offered by broadened investigations of protons with energies below 100 Mev and tests of the effectiveness of pharmaco-chemical radiation defense means under such conditions.

***** THE END *****

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